

Breaking Patterns of Disease

Early-Life Clues May Predict Long-Term Health

Modern diseases often seem to occur in isolation, but many are now known to emerge from a complex web or pattern of conditions linked together by certain underlying biological mechanisms and processes. With the help of large disease databases, medical scientists have begun to discern how such patterns occur over the course of a lifetime. A new review focused on developmental immunotoxicology explores how this integrative perspective might inspire novel strategies for lowering the risk and prevalence of immune-based diseases influenced by environmental stimuli [*EHP* 118(8):1091–1099; Dietert et al.].

Many chronic diseases share three common features: 1) early-life exposures to chemical agents or pathogens, 2) evidence of immune



An Uneven Path Forward

The History of Methylmercury Toxicity Research

Organic mercury compounds were first described in the 1800s, with fatal cases of methylmercury poisoning reported in 1865. Early reports described a distinct set of symptoms of methylmercury toxicity, including altered sensation in the face and extremities, tunnel vision, deafness, loss of coordination, and impaired speech. Nearly a century later, against a backdrop of widespread environmental contamination, the clinical picture reappeared, and suspicions of additional harm to human health had developed. Yet it wasn't until 2009 that international agreement to control mercury pollution was reached. A historical review suggests that—as one early commenter observed—the tunnel vision, forgetfulness, and lack of coordination that symptomize methylmercury toxicity can also affect the conduct and interpretation of environmental health research [*EHP* 118(8):1137–1145; Grandjean et al.].

Methylmercury became commercially important as a crop fungicide around 1914. Worldwide use was accompanied by worker poisonings and several large-scale food poisoning incidents. The compound emerged as an industrial pollutant in the early 1950s around Japan's Minamata Bay, where contaminated seafood induced neurologic symptoms mirroring those reported in 1865. Epidemiologic evidence from Minamata, paired with a 1952 report from Sweden, indicated more severe disease from prenatal and early-life exposures, with symptoms including mental retardation, seizures, and impaired motor development. In the 1960s, advances in analytical technology permitted

insult or dysfunction, and 3) the appearance of disease biomarkers in exposed children although disease itself may not manifest until later in life. One example of interlinked disease conditions highlighted by the authors is metabolic syndrome, defined as the co-occurrence of at least three of five conditions: insulin resistance, obesity, high blood pressure, elevated triglycerides, and reduced HDL cholesterol.

Immune dysfunction is central to the underlying physiology of metabolic syndrome, and the authors posit that the seeds of such dysfunction may be planted in childhood. They describe pre- and postnatal exposures to environmental risk factors that produce postnatal lipid dysregulation and immune dysfunction. However, it is not yet known whether immune dysfunction is an underlying cause of metabolic syndrome or simply an associated or disease-facilitating characteristic.

The practical key to preventing metabolic syndrome may lie in treatments that address overall patterns and their progression, not just the initial presenting condition. “For those patterns of disease with immune involvement,” the authors write, “preventing the underlying immune dysfunction is the single most effective option to minimize the risk of one or more chronic diseases later in life.” This will require more information about risk factors for immune dysfunction that are encountered during development or childhood. Therefore, the authors also recommend that chemicals and pharmaceuticals be tested for developmental immunotoxicity end points; currently, safety assessments are based solely on adult exposures.

The authors say patterns of disease can be used to better predict, prevent, and treat diseases associated with an immune-related pattern of diseases, and may also serve as the basis for environmental protection and testing to prevent exposure to developmental immunotoxicants that may contribute to multiple interconnected diseases. But pattern-based evaluation, prevention, and treatment will require a shift from the prevailing single-organ approach to disease classification and management.

M. Nathaniel Mead, a science writer living in Durham, NC, has written for *EHP* since 2002.

chemical analysis of mercury species in environmental samples, resulting in the discovery of methylmercury biomagnification in the food chain and identification of environmental methylation of inorganic mercury in waterways. Methylmercury had become a worldwide problem, not simply a local issue.

Defining the scope of the problem, much less acting to address it, has involved a political, legal, and ethical maze set on an ever-evolving and still-incomplete scientific foundation. Initially, the inability to identify mercury species in the environment hampered researchers' efforts to link the presence of methylmercury with poisoning symptoms. That link also was blurred by a time lag of weeks to months between exposure and initial symptoms as well as slow recognition of the significance of experimental and wildlife data. Industrial suppression of toxicity data impaired accurate risk assessment, as did imprecise estimates of exposure, delayed recognition of low-dose effects, and use of adult data only.

Consequently, regulatory safeguards established in the 1960s and 1970s are now known to be inadequate, but improvements have been deferred in light of scientific uncertainties. For example, although it remains unknown whether a “safe” threshold exists for prenatal and early-life exposure to methylmercury, evidence of methylmercury damage to neurodevelopment has been accumulating since the 1950s. More research is certainly needed, the authors write, but prevention and correction of environmental health problems need not and should not be delayed by a desire for absolute proof.

Julia R. Barrett, MS, ELS, a Madison, WI–based science writer and editor, has written for *EHP* since 1996. She is a member of the National Association of Science Writers and the Board of Editors in the Life Sciences.